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| EXAMINER | |
|---|---|
| SMITH, CAROLYN L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1631 | |

DATE MAILED: 11/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/865,759 | SHAPIRO, PHYLLIS | |
| | Examiner | Art Unit | |
| | Carolyn L. Smith | 1631 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3 and 5-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's amendments and remarks, filed 9/15/06, are acknowledged. Amended claims 1-2, 7, 9-10, 12, 15-17, and 19 are acknowledged.

Applicant's arguments, filed 9/15/06, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-3 and 5-24 are herein under examination.

### *Claims Rejected Under 35 USC § 112, First Paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

NEW MATTER

Claims 1-3 and 5-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

There does not appear to be written support for the amended limitation "to measure intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another", as stated in instant claims 1 and 9. Applicant

points to support for the amendments on paragraph 0034 of the specification which does not mention anything about measuring concentrations. While the specification (0029) states "the detection and monitoring of an extracellular hemoglobin component, even in the presence of a cellular hemoglobin component derived from the red blood cells in a given sample", this does not state that intracellular hemoglobin concentration is also being measured in the presence of exogenous heme-colored blood substitute. Because the introduction of "to measure intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another" does not have adequate written support in the specification, claims, and/or drawings, as originally filed, this phrase is considered to be NEW MATTER. Claims 2-3, 5-8, and 10-24 are also rejected due to their direct or indirect dependency from claims 1 and 9. This rejection is necessitated by amendment.

### *Claims Rejected Under 35 U.S.C. § 112, Second Paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 16 (line 9) recites the limitation "the automated analyzer" which lacks proper antecedent basis as there is no prior mention of an automated analyzer. Clarification of this issue

via clearer claim wording is requested. Claims 17-22 are also rejected due to their dependency from claim 16.

Claim 16 (lines 19-20) recites the limitation "the plasma hemoglobin value" which lacks proper antecedent basis as there is prior mention of a plasma hemoglobin value. Clarification of this issue via clearer claim wording is requested. Claims 17-22 are also rejected due to their dependency from claim 16.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chupp et al. (P/N 5,631,165) in view of Chang et al. (P/N 5,200,323), Samsoondar (WO 98/39634), and Rodriguez et al. (P/N 6,228,652). This rejection is maintained.

Chupp et al. teach a system where information about the blood sample, generally whole blood which comprises red blood cells (with intracellular hemoglobin), is entered into the controller of an automated system that activates the analyzers, including a hematology analyzer, to perform analyses under the direction of the controller (col. 10, lines 54-67 and col. 12, lines 1-9). Chupp et al. describe tests can be performed on the instrument without separating cells from

the sample during any phase of the analyses (col. 7, lines 40-46) which represents analyzing via a cell hematology analyzer without separating cells from the sample prior to analysis, as stated in instant claims 1 and 9. Chupp et al. describe the system as including an analyzer module, a data station module, and a pneumatic unit (col. 11, lines 27-29). The data station module has "sufficient software algorithms to manipulate measured data, calculate parameters and display results in a variety of formats" (col. 11, lines 62-67). Chupp et al. further discuss the analyzer module in which sample tubes of blood are automatically transported with bar code labels that can be read with a bar code reader so that sample information can be inputted into the system controller (col. 25, lines 22-35) as stated in instant claims 1, 9, 12-13, 15, and 19-20. Chupp et al. teach correcting MCH and MCHC in blood (as stated in instant claims 1, 9, and 21-23) by performing the mathematical computations described in (b) through (e) of instant claim 1 and c(1) – (2) of instant claim 9 where the constants to correct dimension units for formula 1 is 10 and for formula 2 is 100 (col. 53, lines 66-67 and col. 54, lines 1-26), as stated in instant claims 14 and 24. Chupp et al. teach the use of setting hemoglobin flags if any results are abnormal or suspect (col. 61, lines 50-51) which suggests the blood sample tested may be normal or abnormal as stated in claim 3. Chupp et al. also describe anemic patients with increased reticulocyte counts as indicating rapid erythroid turnover suggesting acute blood loss or hemolysis (col. 1, lines 62-65) as stated in claims 5 and 6. However, Chupp et al. do not teach the presence of an extracellular hemoglobin product or oxygen-carrying blood substitute such as recombinant human hemoglobin, isolation and purification from animal blood, subtraction of the blood substitute correction factor from the original reported chemistry result, or cell-by-cell measurements.

Chang et al. describe hemoglobin which carries oxygen to tissues (col. 2, lines 40-43) and the use of modified hemoglobin blood substitutes as alternatives to human donor blood, such as recombinant human hemoglobin (col. 3, lines 61-63) which is an extracellular hemoglobin product or oxygen-carrying blood substitute, as stated in instant claims 2, 7, 10, and 17. Chang et al. describe adding modified hemoglobin blood substitutes to a human plasma sample with a centrifugation step (abstract) which represents isolation and purification of animal blood (as stated in instant claims 8, 11, and 18), as stated in instant claims 1 and 9. Chang et al. do not describe the subtraction of the blood substitute correction factor from the original reported chemistry result or cell-by-cell measurements.

Samsoondar describes a method of identifying and quantifying the concentration of a blood substitute in a sample (abstract). Samsoondar describes a method of taking the measured concentration of the blood substitute and correcting for its effect on a measured analyte concentration, such as serum/plasma total protein (abstract). Samsoondar describes making the necessary adjustment or correction to the measured analyte concentration to remove the effect of the blood substitute (page 5, lines 5-9) which represents a subtraction of the blood substitute correction factor from the original reported chemistry result, as stated in instant claims 16 and 23. Figure 3 (with the linear calibration mathematical formula) provides results of a linear regression fit of data generated from true Hb calibration (fitted Hb value) in the presence of cross-linked hemoglobin (blood substitute) and other interferents (actual Hb value) (page 5, lines 20-22) which represents a correction factor multiplied by the hemoglobin value scaled to the appropriate units of dimensions of the reported analytes to correct for interference, as stated in instant claim 16 and 23. Samsoondar describes quantifying the relationship between measured

amounts of each analyte with respect to the blood substitute present in the serum or plasma specimen (page 18, lines 23-26). In an example, Samsoondar describes finding the actual serum total hemoglobin concentration by subtracting the blood substitute times the slope of the regression line (correction factor) from the measured value (page 23, lines 4-15). Samsoondar describes Hb liberated from blood cells (claim 16). Samsoondar describes determining the concentration of true hemoglobin in the presence of blood substitutes (abstract). Samsoondar describes measuring the concentration of blood substitutes in the presence of Hb (page 3, last paragraph). Samsoondar describes using samples contained in labeled tubes in a blood analyzer (abstract). Samsoondar describes a user can specify a particular interferent to be analyzed (page 11, lines 2-4). Samsoondar describes screening samples by taking successive sample measurements for interferents and blood substitutes (page 11, second paragraph).

Rodriguez et al. describe a blood analyzing instrument (abstract) and taking measurements on every cell where measurement data are processed to yield a report of cells and cellular hemoglobin information including mean volumes for a sample (col. 13, lines 20-33). Rodriguez et al. describe measuring cell-by-cell hemoglobin (col. 13, lines 34-42), as stated in instant claims 1, 9, and 15. Rodriguez et al. describe analyzing whole blood, analyzing subsets of red blood cells (col. 5, line 53 to col. 6, line 51) as well as analyzing only red cells and platelets (col. 6, lines 52-59).

Chupp et al. describe the presence of classes and subclasses of red blood cells (col. 3, lines 53-54) and how the two methods used can distinguish cells and subdivide the cell types into finer classifications (col. 3, lines 7-14). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Chupp et al. by use of an

extracellular hemoglobin product or oxygen-carrying blood substitute, as taught by Chang et al., where the motivation would have been to screen human blood and plasma to determine the safety of modified hemoglobin blood substitutes for humans, as stated by Chang et al. (col. 4, lines 11-30). It would have been further obvious to subtract the blood substitute correction factor from the originally reported chemistry result, as taught by Samsoondar, in the methods of Chupp et al. and Chang et al. where the motivation would have been to determine the concentration of true hemoglobin in the presence of blood substitutes, as stated by Samsoondar (abstract). It would have been further obvious to measure cell-by-cell hemoglobin as taught by Rodriguez et al. in the methods of Chupp et al., Chang et al., and Samsoondar, where the motivation would have been to determine a thorough analysis of a blood sample regarding various blood parameters, as stated by Rodriguez et al. (col. 1, lines 39-47 and col. 13, lines 20-33) by increasing the precision and accuracy of previous manual methods of hematology analysis by using automated systems (Chupp et al., col. 7, lines 11-16), and enhancing the understanding of safety and potential problems of the various types of blood and blood substitutes in humans at the time of the invention, as stated by Chang et al. (col. 4, lines 11-30).

Thus, Chupp et al., in view of Chang et al., Samsoondar, and Rodriguez et al., motivate the limitations in claims 1-3 and 5-24 of the instant invention.

Applicant argues that none of the references teach measuring intracellular hemoglobin in the presence of extracellular heme-colored blood substitutes. This statement is found unpersuasive as Chupp et al. measure intracellular hemoglobin while the other references provide limitations for the extracellular components in the instant claims. For example,

Samsoondar (abstract, page 3, and claim 16). Applicant argues that no reference measures the hemoglobin concentrations having both intracellular hemoglobin and extracellular heme-colored blood substitutes. This statement is found unpersuasive as Chupp et al. measure intracellular hemoglobin while Samsoondar describes measuring true hemoglobin and blood substitutes in the presence of one another (abstract and page 3, last paragraph). Applicant summarizes her invention including a limitation "to measure intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another" which is considered to be NEW MATTER. Applicant summarizes Chupp et al. and argues that they do not have the "measure" limitation as stated above. It is noted that Chupp et al. and Samsoondar teach this limitation. Applicant summarizes Chang et al. and argues that they do not have the "measure" limitation as stated above. It is noted that Chupp et al. and Samsoondar teach this limitation. Applicant summarizes Samsoondar and argues that he does not have the "measure" limitation as stated above because the plasma samples lack cellular hemoglobin because the red cells have been removed. This statement is found unpersuasive as Chupp et al. and Samsoondar teach this limitation. It is noted that "intracellular" can be interpreted to be anything originally from the cell as opposed to a blood substitute that does not originate from the cell (extracellular). Applicant summarizes Rodriguez et al. and argues that they do not teach the "measure" limitation as stated above. It is noted that Chupp et al. and Samsoondar teach this limitation. Applicant summarizes the Rodriguez et al., Chupp et al., and Chang et al. references and argues they teach measuring intracellular hemoglobin and blood substitutes separately. It is noted that not all limitations of a 35 USC 103 rejection need to come from a single reference. It is noted that Samsoondar describes measuring true hemoglobin and blood substitutes in the presence of

one another (abstract and page 3, last paragraph). Applicant argues that no motivation in the prior art has been provided that would lead one of ordinary skill in the art to make the suggested combination. This statement is found unpersuasive as motivational statements from the prior art references themselves are provided for combining the individual references together, as set forth in the rejection above. Applicant's arguments are deemed unpersuasive for the reasons given above.

***Conclusion***

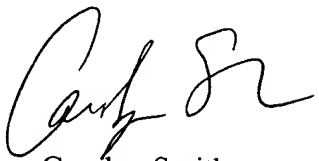
No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811.

November 9, 2006



Carolyn Smith
Examiner
AU 1631